

Prevalence of Asymptomatic Bacteriuria and Associated Host Factors in Women with Diabetes type 2

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Abstract

Background: Asymptomatic bacteriuria (ASB) is common among women with diabetes. The aim of this study was determine the prevalence of and risk factors for ASB in women with diabetes type 2 in Shahre-kord city of Iran.

Methods: In a six months period (April- September 2005), a total of 100 women with diabetes (type 2) and 100 healthy women without diabetes as control group were investigated for the presence of ASB. After a follow-up of six months, the rate of developing of ASB to symptomatic urinary tract infection (UTI) in patients was evaluated.

Results: The prevalence of ASB was 20% in the diabetic patients and 4% in control group ($P < 0.05$). *Escherichia coli*, Coagulase negative staphylococci, *Enterococcus* spp. and *Klebsiella pneumoniae* were the most prevalent isolates respectively. Pyuria was present in 80% of patients with ASB and in 17.5% of those without ASB. Symptomatic UTI in previous year was the only risk factor for ASB in the patients ($P < 0.05$). During a follow-up of six months, 40% of diabetic patients with ASB developed to symptomatic UTI.

Conclusions: The prevalence of ASB is increased in women with diabetes and we recommend screening for detection and treatment of ASB in diabetic patients.

Keywords: Asymptomatic bacteriuria, Diabetes type 2, *Escherichia coli*, Pyuria

Introduction

Diabetes type 2, also known as non insulin-dependent diabetes (NIDDM), is One of the two major types of diabetes in which the beta cells of the pancreas produce insulin but the body is unable to use it effectively because the cells of the body are resistant to the action of insulin (1, 2). Patients with diabetes have an increased risk of infections, with the urinary tract being the most prevalent infection site (2, 3). Besides, the rates of complications of urinary tract infection (UTI)

and upper tract involvement are much higher than in the general population.

Asymptomatic bacteriuria (ASB) in diabetic patients is contributed with increased risk of symptomatic UTI (4, 5). ASB is defined as the presence of at least 10^5 colony-forming units (CFU)/ ml of 1 or 2 bacterial species in clean-voided midstream urine sample from an individual without symptoms of a UTI (1). The prevalence of asymptomatic bacteriuria is about 3 times higher in diabetic women (ranging from 15% to 30%) than in nondiabetic women (less than 10%) (1, 6-8). Local secretion of cytokines and increased adherence of uropathogens to uroepithelial

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cells have been proposed to account for the greater prevalence of bacteriuria in diabetic persons (6, 9). The prevalence of pyuria in young nondiabetic women with ASB is about 32%. This rate in diabetic women is calculated about 70%-80% (10, 11).

Various risk factors for ASB in women with diabetes have been suggested, including sexual intercourse, age, duration, metabolic control, and complications of diabetes (4, 8, 10, 12, 13). Some studies showed that, the number of symptomatic UTI in the previous year increased the risk of developing ASB in diabetic women (14). Mendusa and coworkers (7) postulated that there was no association between fasting glucose concentration and ASB in diabetic women.

Escherichia coli, in diabetic patients, as in others is the most common uropathogen (7, 10). Other Enterobacteriaceae including *Proteus*, *Klebsiella*, *Enterobacter* and *Citrobacter* spp., *Pseudomonas aeruginosa*, *Enterococcus* spp., *Gardnerella vaginalis*, *Streptococcus* and *Staphylococcus* spp., *Candida albicans* and other fungi have been reported (7, 10, 15). The probability of a more severe course of the infection and the proportion of resistant pathogens is also higher in diabetic patients than in nondiabetic patients (4, 6, 16). There is a trend in clinical practice to treat patients with diabetes who have asymptomatic bacteriuria (4). Some studies have not recommended the antibacterial treatment of ASB for prevention of UTI complications in diabetic patients (4, 6, 17). In contrast, other reports have suggested at least 1 course of appropriate antibiotic therapy in an effort to eradicate the pathogen or the postulated pathogen from the urinary tract (1, 11, 15, 18); although in some reports, this is based solely on empiric evidence (18).

Some studies (19) have reported that decreasing renal functional tests is a consequence of ASB in diabetic patients. Geerlings (20) showed that 23% of patients with diabetes type 2 and ASB developed to symptomatic

UTI within 2 mo and postulated that ASB was the most important risk factor for developing UTI in diabetic women. Regarding to these reports and because more UTI complications (e.g., bacteremia, renal abscesses, renal papillary necrosis) are seen in patients with diabetes versus individuals without diabetes (21) and also no published results about ASB especially in diabetic patients in Iran were available, investigating the association between ASB and symptomatic UTI in women with diabetes and need to initiation of therapy in these patients is important.

The aim of the present study, therefore, was to determine the prevalence of and the risk factors for ASB in 100 women with type 2 diabetes in Shahre-kord city (the center of Chahar-mahal Province) of Iran.

Materials and Methods

In a six months period (April- September 2005), and in an analytical cross-sectional study, a total of 100 non-pregnant women with diabetes (type 2) who were 31-81 yr of age and had no abnormalities of the urinary tract and 100 healthy women without diabetes (28-74 yr of age) as control group were included. The groups were matched together demographically. Two groups were investigated for the presence of ASB, which was defined as the presence of at least 10^5 colony forming units/ml of 1 or 2 bacterial species in a culture of clean-voided midstream urine from an individual without symptoms of UTI. Urine samples were kept at 4 °C up to 2 h before culture. The urine was plated onto 5% sheep blood agar (Difco) and MacConkey agar (Difco) plates in two separated plates. A calibrated loop designed to deliver 0.01 ml of urine was used for urine inoculation. For this, the plates were streaked by touching the loop to the center of the plate, from which the inoculum spread in a line across the diameter of the plate. Then, loop was drawn across the entire plate, crossing the first inoculum streak numerous

times to produce isolated colonies. Once plated, urine cultures were incubated at 35 °C. The results were read after 24 h. Colonies were counted on each plate. The number of colony forming units (CFUs) was multiplied by 100 to determine the number of microorganisms per milliliter in the original specimen (22). The presence of WBCs $\geq 10/\text{mm}^3$ of urine was considered as significant pyuria (22). Microorganisms were identified according to standard bacteriologic procedures (22). Exclusion criteria were pregnancy, recent hospitalization or surgery (within the past 4 mo), known urinary tract abnormalities or recent urinary tract instrumentation, symptoms of a UTI (the presence of dysuria, frequency or urgency, abdominal discomfort or fever), or the use of antimicrobial drugs during the previous 14 d. A consent form was filled in by the patients in the beginning of the study. The patients who developed to symptomatic UTI were referred to urologist for further evaluation and initiation of therapy. All patients were interviewed during the first visit of the study and their medical history was obtained using a standardized questionnaire. The questionnaire included age, duration of diabetes, and urinary tract surgery during the previous years and past history of UTIs during the past year. Laboratory values containing serum creatinine, pyuria and fasting glucose concentration were also obtained. During a follow-up of six mo development of ASB into symptomatic upper or lower urinary tract infections were determined. Risk factors were analyzed according to the differences between patients with and those without ASB.

Differences between patients with and without ASB were tested with *t* test for continuous variables (age and duration of diabetes). Chi-square test was used for variables pyuria and number of UTIs during the past year. $P < 0.05$ was considered to be statistically significant. SPSS statistical software for windows (version 11) was used.

Results

Of the total study group ($n = 100$) with type 2 diabetes, 20% had ASB. Only 4% of nondiabetic patients (control group) had ASB ($P < 0.05$). Pyuria was present in 80% of diabetic and 25% of non-diabetic patients with ASB ($P < 0.05$). *Escherichia coli* was isolated in 55% of patients with ASB. Other isolated microorganisms included coagulase-negative *Staphylococcus* spp. (20%), *Enterococcus* spp. (15%), and *Klebsiella pneumoniae* (10%). Eighty percent of diabetic women with ASB and 17.5% of those without ASB had pyuria ($P < 0.05$). Besides, forty percent of diabetic women with ASB had past history of symptomatic UTI in the past year. There was no correlation between age, fasting glucose concentration, duration of diabetes and the presence of ASB in diabetic women. In contrast, significant association was evident between symptomatic UTI during the past year and the presence of ASB in patients ($P < 0.05$) (Table 1). Chi-square test showed that no association was evident between past history of UTI and presence of pyuria. During a follow-up of six mo, 40% (eight patients) of diabetic women with ASB had at least one episode of symptomatic UTI. Five (62.5%) diabetic patients with ASB developed to symptomatic lower UTI (cystitis) and symptomatic upper UTI (pyelonephritis) was detected in three (37.5%) of them. In diabetic patients without ASB, symptomatic lower UTI was detected in only five (6.3%) patients ($P < 0.05$). Upper UTI was not found in these patients. There was an association between age and developing of ASB to symptomatic UTI in our patients ($P = 0.034$). No association was found between duration of diabetes, fasting glucose concentration and developing UTI in diabetic patients with ASB (Table 2). Besides, in our study, no association was found between serum creatinine and presence of ASB in diabetic women.

Table 1: Risk factors for women with diabetes type 2

| Risk factors | ASB+ | ASB- | OR | P |
|--|------------------|-----------------|-------|--------|
| n (%) | 20 (20) | 80 (80) | | |
| Age (yr) | 60.37 +/- 11.8 | 60.37 +/- 11.8 | | 0.14 |
| Duration of diabetes (mo) | 98.87 +/- 89.34 | 73.04 +/- 83.29 | | > 0.05 |
| History of UTIs during the previous year (%) | 40 | 5 | | < 0.05 |
| Fasting glucose concentration (mg/dl) | 205.34 +/- 92.20 | 184.6 +/- 82.8 | 0.165 | |

Data are n (%), means +/- SDs, or Odds Ratios, ASB: Asymptomatic bacteriuria, UTI: Urinary tract infection

Table 2: Risk factors contributed with developing to symptomatic urinary tract infection (UTI) in ASB positive diabetic women.

| Risk factors | ASB + patients Developed to UTI | ASB + patients Not developed to UTI | P |
|---------------------------------------|---------------------------------|-------------------------------------|-------|
| Age (yr) | 56.87 +/- 11.49 | 67.20 +/- 7.36 | 0.034 |
| Duration of diabetes (mo) | 56.63 +/- 94.09 | 73.5 +/- 72.64 | 0.67 |
| Fasting glucose concentration (mg/dl) | 178.13 +/- 79.41 | 222.40 +/- 95.51 | 0.3 |

Data are means +/- SDs, P value, ASB: Asymptomatic bacteriuria, UTI: Urinary tract infection

Discussion

In this study, we found that the prevalence of ASB was higher in women with diabetes than in women without diabetes. In addition, *Escherichia coli* was the predominant microorganism isolated from diabetic patients. These findings were confirmed by other reports (1, 4, 6, 8, 10, 15). Makuyana and co-workers (11) isolated *Staphylococcus aureus*, *Streptococcus* and *Pseudomonas* spp. from diabetic women with ASB. In our study, such isolates were not prevalent.

Although, age has also postulated as the most important risk factor for ASB in type 2 diabetic patients in some reports (14, 23), in the current study we could not find an association between age and the presence of ASB in diabetic women. In contrast, as it is shown in Table 2, age of patients was an important risk factor for developing UTI in diabetic women with ASB. It is shown in this study that, the average of the age in diabetic

women with UTI was lower than patients without UTI. Therefore, it can be concluded that, other factors such as sexual activity and menstrual period in young diabetic women may be included as predisposing factors for developing ASB to symptomatic UTI. This finding has the value for future studies and investigations.

Another risk factor for ASB in type 2 diabetic patients in this study was at least one episode of UTI during the previous year. Previous UTI as a risk factor for ASB indicates that bacteriuria can be present with or without symptoms in the same patient. In some reports (14, 23- 25) the presence of UTI during past year, has also been postulated as important risk factor of ASB in diabetics. It can be concluded that, the colonization of uropathogens in urinary tract of diabetics after episodes of UTI and also local secretion of cytokines and increased adherence of bacteria to uroepithelial cells in these

patients, can accelerate the prolonged release of bacteria from urinary tract which may cause bacteriuria.

Some studies (26) found that diabetic women with ASB had lower urinary cytokine concentrations and therefore decreased urinary leukocyte numbers compared with nondiabetic women with ASB. But, in our study, 80% of women with type 2 diabetes and ASB had pyuria compared to 25% in non diabetic women. The correlation between pyuria and ASB has also been reported by other studies (7, 10, 11, 15). Meiland and associates (19) have reported that decreasing renal functional tests is a consequence of ASB in diabetic patients and therefore, they recommended screening of diabetic patients for ASB. Geerlings (20) showed that 34% of diabetic women with ASB had impaired renal functional tests. In our study, we did not find any association between patients' serum creatinine and presence of ASB.

Some reports (4, 7, 8, 10, 27) have showed that the duration of diabetes is associated with ASB in diabetic patients. In the present study, we could not find any association between duration of diabetes and presence of ASB in diabetes type 2 women. Meiland (14) has also reported that this relationship was not present in patients with diabetes type 2 and only was found between ASB and diabetes type 1.

Geerlings (20) showed that 23% of patients with diabetes type 2 and ASB developed to symptomatic UTI within 2 months and postulated that ASB was the most important risk factor for developing UTI in diabetic women. These findings have been confirmed by Ooi and coworkers (4). In this study, after a six months follow-up of diabetic women with ASB, a considerable percentage of patients, developed to symptomatic UTI. Therefore, we can conclude that ASB could be considered an essential risk factor for developing UTI in diabetic patients.

No consensus exists regarding the treatment of ASB in diabetic patients. Many experts recommend treating ASB in diabetic patients because of the frequency and severity of upper UTIs (6, 23, 28). On the other hand, some studies believe that the benefit of treatment is doubtful (4, 29). This contrast is believed as a lack of follow-up studies of diabetic women with untreated ASB. In this study, as mentioned above, after a six months follow-up of diabetic women with ASB, 40% developed to symptomatic UTI. Therefore, although a further investigation about approach in diabetic patients with ASB is suggested, based on our findings, we recommend screening and treatment of ASB in diabetic women.

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